

REMARKS

Claims 1-34, 47, 48, 50-55, and 64-103 were pending in the application. Claims 1, 4-6, 8-10, 16, 19, 24, 27, 31, 34, 47, 48, 50, and 65 have been amended, claims 104-111 have been added, and claims 2, 3, 11-15, 20-23, 28-30, 32, 33, 64, and 66-103 have been cancelled. Accordingly, claims 1, 4-10, 16-19, 24-27, 31, 34, 47, 48, 50-55, 65, and 104-111 will be pending in the application upon entry of the instant claim amendments and additions presented herein. A "Version With Markings to Show Changes Made" setting forth amendments to the specification and claims as presented herein is attached hereto as Appendix A.

Support for the amendments to claims 1, 4-6, 8-10, 16, 19, 24, 27, 31, 34, 47, 48, 50, and 65 may be found in the claims as originally filed and throughout the specification. Specifically, support for the amendment to claim 1 can be found in claims 2 and 15 as previously examined; support for claim 16 can be found in claim 15 as originally examined; support for claim 19 can be found in claims 22 and 28 as originally examined; support for claim 24 can be found in claim 4 as originally examined; support for claim 27 can be found in claim 5 as originally examined; support for claims 47, 48, and 50 can be found in claim 76 as originally filed; and support for claim 65 can be found in claim 64 as originally filed. No new matter has been added by these amendments. Amendment or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite prosecution. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Objection to the Title

The title is objected to as not being "aptly descriptive". The Examiner states that "[a] new title is required that is clearly indicative of the invention to which the claims are directed."

Applicants respectfully submit that this objection is moot in view of Applicants' amendment to the title.

Objection to the Abstract

The abstract is objected to as not being "directed to the claimed invention".

Applicants respectfully submit that this objection is moot in view of Applicants' amendment to the abstract.

Rejection of Claims 1-34, 47, 48, 50-55, and 64-103 Under Obviousness-Type Double Patenting

Claims 1-34, 47, 48, 50-55, and 64-103 are objected to "under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,037,138."

Applicants will file a terminal disclaimer upon the indication of allowable subject matter, if appropriate.

Rejection of Claims 1-34, 47, 48, 50-55, and 64-103 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-34, 47, 48, 50-55, and 64-103 under 35 U.S.C. § 112, first paragraph because, according to the Examiner, "the specification, while possibly being enabling for specific enzymes and prostate cancer, does not reasonably provide enablement for "a matrix digesting enzyme" or "cancer". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims."

Claims 2, 3, 11-15, 20-23, 28-30, 32, 33, 64, and 66-103 have been canceled without prejudice. Therefore this rejection is moot with regard to claims 2, 3, 11-15, 20-

23, 28-30, 32, 33, 64, and 66-103. To the extent this rejection applies to amended claims 1, 4-6, 8-10, 16, 19, 24, 27, 31, 34, 47, 48, and 50, Applicants traverse.

Claim 1 and dependent claims 4-10, 16-19, 24-27, 31, 34, 47, 48, 50-55, and 65 as amended, are drawn to non-invasive methods for facilitating the diagnosis of a subject for cancer, comprising obtaining a *urine sample* from a subject, detecting the presence or absence of a *matrix metalloproteinase in the urine sample*, and correlating the presence or absence of the matrix metalloproteinase with the presence or absence of cancer, thereby facilitating the diagnosis of the subject for cancer. Thus, the pending claims all require that cancer is diagnosed by detecting the presence or absence of a matrix metalloproteinase in the urine of a patient.

It is Applicant's position that one of skill in the art could easily practice the claimed methods without undue experimentation. Applicants' specification teaches methods of detecting various kinds of cancer. For example, Applicants teach, at least at page 18 line 22 to page 20 line 4 of the specification, the preparation of urine samples for analysis, as well as methods to detect matrix metalloproteinases in the urine samples by sodium dodecyl sulfate polyacrylamide gel electrophoresis and zymography. Furthermore, Applicants disclose working examples whereby Applicants detect the presence of matrix metalloproteinases in the urine of subjects that have various forms of cancer. At least at Example 2 of the specification, Applicants teach the detection of metastatic cancer, bladder cancer, renal cancer, testicular cancer, lymphoma, and pheochromocytoma by detecting matrix metalloproteinases in the urine of patients presenting with each type of cancer. Thus, one of ordinary skill in the art, armed with the teachings of the specification and the knowledge of the art, would be able to make and use the invention as claimed.

In view of the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the foregoing section 112, first paragraph rejection.

Rejection of Claims 1-34, 47, 48, 50-55, and 64-103 Under 35 U.S.C. § 112, Second Paragraph

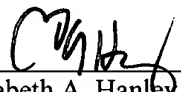
The Examiner has rejected claims 1-34, 47, 48, 50-55, and 64-103 under 35 U.S.C. § 112, second paragraph because, according to the Examiner, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner states that "[i]n claim 1, the detecting step implies that something is detected which may or may not be the case. Determining is a more standard term. In claim 48, 81 the MW reads on an infinite weight."

Applicants respectfully submit that these rejections have been rendered moot in view of Applicants' amendments and cancellations. Claim 1 has been amended to recite "detecting the presence or absence of". Claim 48 has been amended to remove "equal to or greater than" so the claim recites "a molecular weight of approximately 150 kDa." Claim 81 has been cancelled. In view of the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the foregoing section 112, second paragraph rejection.

CONCLUSION

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



Elizabeth A. Hanley
Registration No. 33,505
Attorney for Applicants

28 State Street
Boston, MA 02109
Tel. (617) 227-7400
Dated: June 5, 2001

Appendix A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The specification as originally filed has been amended as follows:

At pages 1 and 40, the title has been replaced as follows:

NON-INVASIVE ENZYME SCREEN FOR CANCER ~~TISSUE REMODELLING-
ASSOCIATED CONDITIONS~~

At page 40, lines 7-11 have been replaced as follows:

Methods and kits for diagnosing the presence of ~~and prognosing the appearance of~~
~~tissue remodelling-associated conditions~~ cancer, involving the presence of enzymes in a
biological sample, are disclosed. In particular, the methods pertains to diagnosing the
presence of ~~or prognosing appearance of~~ various forms of cancer, metastatic cancer, and
~~obstructive and degenerative conditions.~~

In the claims:

Claims 1, 4-6, 8-10, 16, 19, 24, 27, 31, 34, 47, 48, 50, and 65 have been amended
as follows:

1. (Amended) A non-invasive method for facilitating the diagnosis of a
subject for cancer ~~a tissue remodelling-associated condition~~, comprising:
obtaining a urine sample from a subject;
detecting the presence or absence of a matrix metalloproteinase [~~an~~
~~enzyme~~ in the urine sample; and
correlating the presence or absence of the matrix metalloproteinase
~~enzyme~~ with the presence or absence of cancer ~~a tissue remodelling-associated condition~~,
thereby facilitating the diagnosis of the subject for cancer ~~the tissue remodelling-
associated condition~~.

4. (Amended) The method of claim 1 ~~2~~, wherein the cancer is organ-
confined prostate cancer.

5. (Amended) The method of claim 1 ~~2~~, wherein the cancer is metastatic prostate cancer.

6. (Amended) The method of claim 1 ~~2~~, wherein the cancer is in cells of epithelial origin.

8. (Amended) The method of claim 1 ~~2~~, wherein the cancer appears in cells of mesodermal origin.

9. (Amended) The method of claim 1 ~~2~~, wherein the cancer appears in cells of endodermal origin.

10. (Amended) The method of claim 1 ~~2~~, wherein the cancer affects cells of bone or of hematopoietic origin.

16. (Amended) The method of claim 1, wherein the matrix ~~-digesting enzyme~~ metalloproteinase is a proenzyme.

19. (Amended) A non-invasive method for facilitating the diagnosis of a subject for ~~a disorder of the prostate cancer~~, comprising:
 obtaining a urine sample from a subject; and
 detecting a ~~prostate disorder-associated enzyme~~ matrix metalloproteinase in the urine sample, thereby facilitating the diagnosis of the subject for ~~the prostate cancer disorder~~.

24. (Amended) The method of claim 19, wherein the ~~disorder of the prostate cancer~~ is organ-confined prostate cancer.

27. (Amended) The method of claim 19, wherein the prostate cancer ~~disorder~~ is metastatic cancer.

31. (Amended) The method of claim 19 ~~30~~, wherein the matrix metalloproteinase is gelatinase A or gelatinase B.

34. (Amended) The method of claim 19 ~~28~~, further comprising removal of low molecular weight contaminants from the urine prior to the detection step.

47. (Amended) The method of claim 1, wherein the matrix metalloproteinase enzyme has a molecular weight of approximately 72 kDa or approximately 92 kDa.

48. (Amended) The method of claim 1, wherein the matrix metalloproteinase enzyme has a molecular weight [equal to or greater than] of approximately 150 kDa.

50. (Amended) The method of claim 1, wherein the matrix metalloproteinase enzyme is detected electrophoretically.

65. (Amended) The method of claim 1 ~~64~~, wherein the cancer is breast cancer.